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(71) Applicant: THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK [US/US]; West 116th Street and Broadway, New York, NY 10027 (US).

(72) Inventors: CHANG, Yuan; 20 Quarry Lane, Irvington, NY 10533 (US). BOHENZKY, Roy, A.; Apartment 115, 870 East El Camino Real, Mountain View, CA 94040 (US). RUSSO, James, J.; Apartment 25E, 60 Haven Avenue, New York, NY 10032 (US). EDELMAN, Isidore, S.; Apartment 61, 464 Riverside Drive, New York, NY 10027 (US). MOORE, Patrick, S.; 20 Quarry Lane, Irvington, NY 10533 (US).

(74) Agent: WHITE, John, P.; Cooper & Dunham LLP, 1185 Avenue of the Americas, New York, NY 10036 (US).

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(54) Title: UNIQUE ASSOCIATED KAPOSI'S SARCOMA VIRUS SEQUENCES AND USES THEREOF

(57) Abstract

This invention provides an isolated nucleic acid molecule which encodes Kaposi's Sarcoma-Associated Herpesvirus (KSHV) polypeptides. This invention provides an isolated polypeptide molecule of KSHV. This invention provides an antibody specific to the polypeptide. Antisense and triplex oligonucleotide molecules are also provided. This invention provides a vaccine for Kaposi's Sarcoma (KS). This invention provides methods of vaccination, prophylaxis, diagnosis and treatment of a subject with KS and of detecting expression of a DNA virus associated with Kaposi's sarcoma in a cell.

What is claimed is:

1. An isolated nucleic acid encoding a Kaposi's sarcoma-associated herpesvirus polypeptide selected from the group comprising:
   a. viral macrophage inflammatory protein II;
   b. viral interleukin 6;
   c. viral interferon regulatory factor 1;
   d. complement-binding protein;
   e. glycoprotein B;
   f. capsid protein IV encoded by ORF 65;
   g. immediate early protein encoded by ORF 73;
   h. glycoprotein M; and
   i. glycoprotein L.

2. The synthetic DNA of claim 1.

3. The genomic DNA of claim 1.

4. The cDNA of claim 1.

5. The RNA of claim 1.

6. A replicable vector comprising the nucleic acid of claim 1.

7. A host cell comprising the vector of claim 6.

8. The eukaryotic cell of claim 7.

9. The bacterial cell of claim 7.

10. A plasmid, cosmid, λ phage or YAC comprising the isolated nucleic acid of claim 1.

11. A nucleic acid of at least 14 nucleotides capable of specifically hybridizing with the isolated

of specifically hybridizing with the isolated nucleic acid of claim 1.

12. The nucleic acid of claim 11 which is labeled with a detectable marker.

13. The nucleic acid of claim 12, wherein the marker is a radioactive, a colorimetric, a luminescent, or a fluorescent label.

14. An isolated polypeptide having the amino acid sequence encoded by the nucleic acid of claim 1.

15. The polypeptide of claim 14 linked to a second polypeptide to form a fusion protein.

16. The fusion protein of claim 15, wherein the second polypeptide is beta-galactosidase.

17. An antibody which specifically binds to the polypeptide of claim 14.

18. The antibody of claim 17, wherein the antibody is polyclonal antibody.

19. The antibody of claim 17, wherein the antibody is a monoclonal antibody.

20. A host cell which expresses the polypeptide of claim 14.

21. A vaccine which comprises an effective immunizing amount of the polypeptide of claim 14 and a pharmaceutically acceptable carrier.

22. An antisense molecule capable of specifically

hybridizing with the nucleic acid of claim 1.

23. The antisense molecule of claim 22, wherein the molecule is a nucleic acid derivative.

24. A triplex oligonucleotide capable of specifically hybridizing with the double-stranded nucleic acid of claim 1.

25. A transgenic nonhuman mammal which comprises the nucleic acid of claim 1 introduced into the mammal at an embryonic stage.

26. A method of diagnosing a DNA virus associated with Kaposi's sarcoma in a subject which comprises:

(a) obtaining a nucleic acid sample from the subject;

(b) contacting the sample obtained in step (a) with the labeled nucleic acid of claim 12 under high stringency hybridization conditions;

(c) detecting the presence of any labeled nucleic acid hybridized in step (b), the presence of which is indicative of a DNA virus associated with Kaposi's sarcoma,

so as to thereby diagnose a DNA virus associated with Kaposi's sarcoma in the subject.

27. The method of claim 26, wherein the sample comprises a bodily fluid.

28. The method of claim 27, wherein the bodily fluid comprises serum.

29. The method of claim 26, wherein the sample comprises a tissue specimen.

30. The method of claim 29, wherein the tissue specimen comprises a tumor lesion.

31. The method of claim 26 wherein the nucleic acid is amplified before step (b).

32. A method of diagnosing a DNA virus associated with Kaposi's sarcoma in a subject which comprises:

(a) obtaining a sample from the subject;

(b) contacting the sample from step (a) with a support having already bound thereto the Kaposi's sarcoma antibody of claim 17, so as to bind the antibody to any specific Kaposi's sarcoma antigen present in the sample;

(c) removing any unbound material from the support of step (b); and

(d) detecting the presence of any specific Kaposi's sarcoma antigen bound by the Kaposi's sarcoma antibody in step (c), the presence of which is indicative of the DNA virus associated with Kaposi's sarcoma,

so as to thereby diagnose the DNA virus associated with Kaposi's sarcoma in the subject.

33. The method of claim 32, wherein the sample comprises a suitable bodily fluid.

34. The method of claim 33, wherein the bodily fluid comprises serum.

35. A method of diagnosing a DNA virus associated with Kaposi's sarcoma in a subject which comprises:

(a) obtaining a suitable bodily fluid sample from the subject;

(b) contacting the sample from step (a) to a support having already bound thereto a Kaposi's sarcoma antigen encoded by the isolated nucleic acid of claim 1, so as to bind the antigen to any specific Kaposi's sarcoma antibody present in the sample;

(c) removing any unbound material from the support of step (b); and

(d) detecting the presence of any specific Kaposi's sarcoma antibody bound by the Kaposi's sarcoma antigen in step (c), the presence of which is indicative of the DNA virus associated with Kaposi's sarcoma,

so as to thereby diagnose the DNA virus associated with Kaposi's sarcoma in the subject.

36. The method of claim 35, wherein the sample comprises a suitable bodily fluid.

37. The method of claim 36, wherein the bodily fluid comprises serum.

38. A method of treating a subject infected with Kaposi's sarcoma- associated herpesvirus comprising administering to the subject an effective amount of an antisense molecule of claim 22 under conditions such that the antisense molecule selectively enters an infected cell of the subject, so as to thereby treat the subject.

39. A method of treating a subject infected with Kaposi's sarcoma- associated herpesvirus comprising administering to the subject a pharmaceutically effective amount of an antiviral agent in a pharmaceutically acceptable carrier, wherein the agent specifically binds to the polypeptide of claim 14.

40. A method of prophylaxis or treatment for a subject infected with Kaposi's sarcoma-associated herpesvirus comprising administering to the subject the antibody of claim 17 in a pharmaceutically acceptable carrier.

41. A method of vaccinating a subject against Kaposi's sarcoma- associated herpesvirus comprising administering to the subject an effective amount of the polypeptide of claim 14 and a pharmaceutically acceptable carrier, so as to thereby vaccinate the subject.

42. A method of immunizing a subject against a herpesvirus associated with Kaposi's sarcoma which comprises administering to the subject an effective immunizing dose of the vaccine of claim 21 and a pharmaceutically acceptable carrier.

43. The antibody of claim 18, which antibody is specifically immunoreactive with peptides encoding an antigenic portion of viral interleukin 6.

44. The antibody of claim 43, wherein the antigenic portion of viral interleukin 6 comprises the amino acid sequences as set forth in SEQ ID NO:2 and SEQ ID NO:3.

45. The method of claim 40, wherein the antibody is a chimeric antibody.

46. The method of claim 40, wherein the antibody is a humanized antibody.

47. A method of passively immunizing a subject against a herpesvirus associated with Kaposi's

sarcoma which comprises administering to the subject an effective immunizing amount of the antibody of claim 43 and a pharmaceutically acceptable carrier.

5